impermeable backing layer, said active substance being dispersed in the preparation to form the polymer matrix layer, and said self-adhesive polymer matrix layer making it unnecessary to affix the transdermal therapeutic patch to the skin via an additional adhesive means, whereby said transdermal therapeutic patch provides treatment of plasma lipid levels, especially in the case of systemic lipid metabolism disturbances, so-called hyperlipoproteinemias and vascular diseases such as cardiac infarction, as well as occlusive arterial disease.

REMARKS

The Office action dated November 5, 2001 is acknowledged. Claims 1-14 are pending in the instant application. According to the Office action, claims 1-14 have been rejected. By the present "Reply to First Office Action," claim 1 has been amended and it, and the claims depending therefrom, are now believed to be allowable. Reconsideration is respectfully requested in light of the amendments being made herein and of the following remarks. No new matter has been added.

Rejection of Claims 1 Under U.S.C. 112, Second Paragraph

Claim 1 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner states that the term "lipid blood levels" in claim 1 is a relative term not being defined by the claim and not having a standard in the specification by which one of ordinary skill in the art would be reasonably apprised of the scope of the invention.

Applicant has adopted the Examiner's suggestion and has replaced the term "lipid

blood levels" in claim 1 with the term "blood lipid levels." As amended, claim 1 meets the requirements f 35 U.S.C. 112, second paragraph. Therefore, it is respectfully submitted that the rejection under 35 U.S.C. 112, second paragraph be withdrawn.

Rejection of Claims 1-14 under 35 U.S.C. 103 (a)

Claims 1-14 have been rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,503,844 (Kwiatek et al.) or U.S. Patent No. 5,066,494 (Becher). It is respectfully submitted that these claims are patentably distinct from the prior art.

Examiner states that Kwiatek et al. '844 suggests the use of a transdermal therapeutic patch for the controlled release of lovastatin to the skin or mucuous membrances and that Kwiatek et al. '844 suggests all of the claimed limitations, but does not expressly suggest the use of a patch in which the active substance is contained within a self-adhesive matrix layer; but rather in foam, which requires a laminate to be affixed onto the skin or mucosa for the release of the active agent. Examiner further states that Becher '494 suggests the use of a transdermal therapeutic patch comprising a contact adhesive layer as a means of fixing the therapeutic system onto human skin. Therefore, Examiner concludes, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a therapeutic patch delivery system consisting of an adhesive layer as a means for affixing the therapeutic composition onto the skin of a patient. This in turn, according to the Examiner, would result in a transdermal patch that adheres well to the skin and offers administration of the active substance.

Applicant submits that the present invention concerns a transdermal therapeutic system (TTS) containing an active substance that l wers the blood lipid levels in a self-

adhesive matrix layer, as stated in the specification at page 5, lines 9-16. In other words, the present invention is a matrix system that is essentially based on an active substance being contained in a polymer matrix. In such a system, it is the polymer matrix that controls the release of the active substance. Furthermore, the active substance containing polymer matrix is self-adhesive and therefore it is not necessary to provide an active substance containing matrix layer having an additional adhesive coating in order to affix the TTS to the patient's skin.

Applicant submits that the transdermal therapeutic system as taught by Kwiatek et al. '844 teaches a reservoir system having a foam laminate transdermal patch, as explained in the Abstract. Applicant submits that such a patch employing a foam laminate would have the same disadvantages as those discussed in the specification at page 4, lines 8-20, namely adhering poorly to the patient's skin and having poor flexibility relative to the patient's skin. Applicant further submits that such a system has the active substance incorporated into the foam layer via soaking (Col. 3, lines 18-34), for example, and the active substance therefore must be liquid, at least during application.

Yet another drawback to this method is that such a foam is unable to control the flux of the active substance from the patch onto and through the skin. In the Abstract, Kwiatek et al. '844 specifically teaches the use of an additional adhesive means in order to secure the foam layer to the patient's skin (see also Col. 5, lines 42-46). This can be achieved by coating the surface of the foam layer facing the skin with an adhesive or by providing the surface of the foam layer facing away from the skin with an adhesive film that projects peripherally beyond the foam layer to provide a frame-like adhesive means

(Col. 5, lines 42-63). It is important to note that the former coating must not impair the release of the active substance from th patch. The latter method does not ensure contact of the entire drug-releasing surface of the patch to the patient's skin during application, which may lessen the therapeutic efficiency of the TTS.

Applicant also submits that Becher '494 relates to a transdermal therapeutic system comprising a multi-chamber active substance depot and a contact adhesive means for affixing the system to the skin of a patient (see Abstract). Applicant further submits that although the contact adhesive means may serve to distribute the active substance, the adhesive means corresponds to the adhesive layer of the patches according to Kwiatek et al. '844, as shown in Figures 1-5, 9a, 10 and 11. Therefore, Becher '494 does not provide any information in addition to the disclosure of Kwiatek et al. '844 which would lead a person skilled in the art towards the present invention since both references suggest how to affix an otherwise non-adhesive system to a patient's skin by using an additional adhesive means.

Applicant respectfully submits that even if a person skilled in the art would consider Kwiatek et al. '844 and Becher '494, alone or in combination with each other, the device of the present invention would still not result. The references teach transdermal therapeutic systems that require an additional adhesive means to be employed in order to affix the TTS to the patient's skin (see Kwiatek et al. '844 Abstract and Becher '494 Abstract). The TTS of the present invention does not require any additional adhesive means because the active substance containing matrix itself is made of an adhesive polymer that is able to efficiently release the active substance onto and through

the patient's skin. Furthermore, neither Kwiatek et al. '844 or Becher '494 teach or suggest in any way to disperse the active substance in an adhesive polymer to generate a matrix system. Therefore, the teachings of Kwiatek et al. '844, even in combination with Becher '494, could not provide sufficient guidance for inventing a device that is characterized by the combination of essential features specified in the present invention.

Applicant respectfully submits that claim 1 has been further amended to specifically recite the feature of having a TTS not needing an additional adhesive means to be adhered to the patient's skin and having a TTS that disperses the active substance in an adhesive polymer to generate a matrix system. Therefore, Applicant respectfully requests that this rejection be withdrawn. No new matter has been added.

For the foregoing reasons, it is respectfully submitted that the present application is in condition for allowance, and such action is earnestly solicited. The Examiner is invited to call the undersigned if there are any remaining issues to be discussed which could expedite the prosecution of the present application.

Respectfully submitted,

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Enc. – Marked Up Claims, Clean and Marked-Up Replacement Paragraphs, Clean and Marked-Up Replacement Abstract
DPH/sm

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on January 24, 2002

Sean Mellum

Dated: Jan. 24, 2002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Achim Berthold
Serial No.	:	09/743,292
Filing Date	:	March 27, 2001
Examiner	:	Humera Sheikh
Group Art Unit	:	1615
Title	:	Transdermal Plaster Containing at Least One Active Ingredient which Influences Blood Serum Levels
Attorney File	:	RO0212US (#90568)

Box Non-Fee Amendment
Commissioner for Patents
Washington D.C., 20231

Marked-Up Amended Claims Under CFR 1.121(c)(1)(ii)

1. (Twice Amended) A preparation containing at least one active substance having an influence on the [lipid blood levels] blood lipid levels of an organism, wherein said preparation is present in the form of a transdermal therapeutic patch containing the active substance in a self-adhesive polymer matrix layer which can be covered at the side facing away from the skin with an active substance-impermeable backing layer, said active substance being incorporated in the preparation to form the polymer matrix layer, and said self-adhesive polymer matrix layer making it unnecessary to affix the transdermal therapeutic patch to the skin via an additional adhesive means.

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on January 24, 2002 (19)

Sue Mellinger

Dated: Jan. 24, 2002

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Marked-Up Replacement Paragraphs Under CFR 1.121 (b)(1)(iii)

1. Systemic lipid metabolism disturbances, especially so-called hyperlipoproteinemias, are of great significance in the pathogenesis of arteriosclerotic vascular diseases and of their consequences, such as cardiac infarction, apoplectic insultus and occlusive arterial diseases. In the USA and Europe about 15 percent of adults have an increased risk of suffering cardiovascular incidents because of increased lipid levels in the blood. A sensible starting point for prophylaxis, therapy and the treatment of consequences consists [in] of lowering increased plasma lipid levels. The [Basis] basis for any treatment of hyperlipoproteinemia is an appropriate diet. A normalization of weight, appropriate diet composition, a proportion of fat <30% of the total number of calories, a sufficient dietary fiber intake, and a reduced cholesterol intake, especially <300 mg per day, must be ensured. Furthermore it is advisable to increase the

intake of unsaturated – above all monounsaturated – fatty acids, since these improve the metabolism of lipoproteins. If by dietary measures alone it is not possible to achieve a sufficient normalization of the lipid blood level and if this means a higher risk of arteriosclerosis, lipid-lowering medicaments are indicated in addition. By treatment with lipid-lowering medicaments a marked reduction of these diseases can be achieved. Current studies, e.g. LCAS – Lipoprotein and Coronary Arteriosclerosis Study; LIPID – Long-term Intervention with Pravastatin in Ischemic Disease; CARE – The Cholesterol and Recurrent Events Trial, were able to show that drug therapy for prevention of ateriosclerotic vascular diseases is effective even where the [lipid blood] blood lipid levels prior to treatment are only slightly increased or even within the normal range.

2. Starting from the above-mentioned prior art, the invention has the object of providing a preparation containing at least one active substance which has an influence on the [lipid blood] blood lipid levels of an organism, by which [preparation] it is possible to achieve a release of the therapeutically active substance which takes place at a constantly low rate over prolonged periods of time and which can be accurately dosed. [, and which preparation, in] In particular, the preparation guarantees absolute bioavailability of the substance while affording a user-friendly mode of application, and [with the said preparation] while serving as an active substance reservoir.

3. To achieve this object, in a preparation containing at least one active substance having an influence on the [lipid blood] blood lipid levels of an organism, it is proposed by the invention that the [said] preparation be present in the form of a transdermal therapeutic patch (TTS) containing the active substance in a self-adhesive matrix layer

which on side facing away from the skin can be covered with an active substance-impermeable backing layer.

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Sean Mellin

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